Abstract only

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The lung-specific surfactant protein B gene promoter is a target for thyroid transcription factor 1 and hepatocyte nuclear factor 3, indicating common factors for organ-specific gene expression along the foregut axis.

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We used the lung epithelial cell-specific surfactant protein B (SPB) gene promoter as a model with which to investigate mechanisms involved in transcriptional control of lung-specific genes. In a previous study, we showed that the SPB promoter specifically activated expression of a linked reporter gene in the continuous H441 lung cell line and that H441 nuclear proteins specifically protected a region of this promoter from bp -111 to -73. In this study, we further show that this region is a complex binding site for thyroid transcription factor 1 (TTF-1) and hepatocyte nuclear factor 3 (HNF-3). Whereas TTF-1 bound two highly degenerate and closely spaced sites, HNF-3 proteins bound a TGT3 motif (TGTTTGT) that is also found in several liver-specific gene regulatory regions, where it appears to be a weak affinity site for HNF-3. Point mutations of these binding sites eliminated factor binding and resulted in significant decreases in transfected SPB promoter activity. In addition, we developed a cotransfection assay and showed that a family of lung-specific gene promoters that included the SPB, SPC, SPA, and Clara cell secretory protein (CCSP) gene promoters were specifically activated by cotransfected TTF-1. We conclude that TTF-1 and HNF-3 are major activators of lung-specific genes and propose that these factors are involved in a general mechanism of lung-specific gene transcription. Importantly, these data also show that common factors are involved in organ-specific gene expression along the mammalian foregut axis.

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